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**IL-1β induces rapid secretion of the antimicrobial protein IL-26 from Th17 cells**

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Th17 cells play a fundamental role in both immunity and autoimmunity at mucosal surfaces, including skin. Recent work has implicated the Th17 cytokine IL-26 as directly antimicrobial to extracellular and intracellular bacteria, including Mycobacterium leprae, the causative agent of leprosy. IL-26 protein expression was greater in skin lesions from patients with the resistant vs. progressive form of the disease. To characterize the mechanism of IL-26 induction, we examined the kinetics of IL-26 secretion from PBMCs exposed to Mycobacterium leprae spesionate, which revealed significant release at 3 hours, reminiscent of an innate response. Pattern recognition receptor ligands induced IL-26 secretion from PBMC, which was mediated by IL-1β. Reconstituent IL-1β alone was sufficient to stimulate IL-26 release from PBMC and human dermal microvascular endothelial cells (HMEC). IL-1β stimulated IL-26 secretion more rapidly from memory CD4+ T cells as compared to TCR activation with crosslinking antibodies. Further investigation revealed that IL-1RI expression was necessary for IL-1β-induced IL-26 from memory Th17 cells. IL-1β stimulation did not lead to secretion of other Th17 cytokines, unlike TCR activation. RNA sequencing of IL-1β-treated IL-1RI-/- Th17 cells revealed enrichment for NF-κB regulated genes. Inhibition of NF-κB signaling with Bay 11-7082 abrogated IL-26 production in response to either stimulus. Finally, supernatants from IL-1β treated memory T cells showed antimicrobial activity against E. coli in an IL-1β-dependent manner. Together, these results identify IL-1RI+ Th17 cells as an antimicrobial Th17 subpopulation with the ability to rapidly respond to IL-1β and induce IL-26 to kill extracellular bacteria.

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**CBFβ is required for LC hemostasis and repopulation but not required for its embryonic development**

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LCs are the sole dendritic cell subpopulation in the epidermis and potent regulators of immune surveillance and tolerance. Unlike conventional DCs, LCs follow unique patterns of development and maintenance under steady and inflamed states. Several transcription factors are essential for LC differentiation, including Runc1, which functions by forming heterodimers with the non-DNA binding I-Subunit (CBFβ) (Core-Binding Factor Subunit Beta) 1 or 2. However, the roles of CBFβ in LCs have not been characterized due to both embryonic lethality and genetic redundancy. It is not known to address if CBFβ is required for LC development, we generated Csf1r.CBFb2-KO mice in which CBFβ2 is deficient in macrophage/monocytes and LC precursors from embryonic stage. We found that the specific deletion of CBFβ in CSF1R expressing cells resulted in a significant decrease in the number of LCs in adult mice compared to WT littermates, while there was no significant difference on LC precursors at embryonic E17.5 and P0 between the CBFβ2 deficient and WT controls. Furthermore, the conditional deletion of CBFβ2 dramatically blocked BM-derived MHCII+ LCs' long-term LC repopulation after exposure to UV-C treatment. Thus, our data highly suggest that CBFβ is required for LCs self-renewing at steady state and controls LC repopulation at inflammatory state, but not required for its embryonic development.

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**Psoriatic fungal and bacterial microbiota identifies patient endotypes**

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Psoriatic arthritis (PsA) is a chronic, inflammatory disease characterized by immune-driven keratinocyte hyperplasia. We report identification of pro- and anti-inflammatory intestinal microbiota clusters, bacterial and fungal, in psoriatic patients versus healthy controls. We also examined the association between disease severity and the microbiota of psoriasis skin. Fecal and skin samples were obtained from 67 psoriatic patients and 12 healthy controls. Disease severity was assessed by body surface area, 16S (bacterial) and ITS1 region (fungal) genes were amplified and then sequenced using an Ion Torrent S5 system. Relative abundance was determined using non-parametric comparisons. Interestingly, fungal samples showed a pattern of intestinal dysbiosis similar to that previously reported for Crohn’s disease (CD) patients. Clusters of psoriasis endotypes were identified by intestinal dysbiosis favoring proinflammatory and fungal pathogens. There was a significant increase in Staphylococcus, Serratia, and Enterobacter (p < 0.0267, 0.00029, 0.0076, respectively) as well as fungi including C. albicans and C. Parapsilosis (p = 0.0286 and 0.0316, respectively) in the gut compared to healthy controls. These data were consistent with their beneficial anti-inflammatory properties such as F. prausnitzii and Clostridium were markedly reduced. Similar clustering was observed at the skin level, where we report for the first time a positive correlation between disease severity and increased abundance of the proinflammatory and fungal pathogens, S. aureus, and C. parapsilosis. The proinflammatory and anti-inflammatory role of these three organisms has also been described in the gut of CD patients suggesting a potential link between the microbiota of CD and PsO.

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**Systemic sphingosine 1-phosphate receptor 2 (S1PR2) deficiency facilitates dermal neutrophil infiltration against S. aureus infection**

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Atopic dermatitis (AD) is an inflammatory, relapsing, itchy skin disease that affects 15-30% of children and up to 5% of adults. AD patients exhibit elevated serum IgE and Staphylococcus aureus colonization on lesional skin that correlates with disease severity. We previously discovered that S. aureus induces IL-36-dependent AD-like skin inflammation. However, it is unclear what role S. aureus has on anti-IgE responses. Herein, we used a S. aureus epi-cutaneous infection model to mimic AD skin inflammation and examine the immune mechanisms of IgE production. Interestingly, epicutaneous S. aureus infection promoted IL-36-dependent IgE responses and plasma cell populations. Treatment with an anti-mouse S1P receptor 2 (S1PR2) antibody induced a significant decrease in filaggrin2. These data suggest that, although the lack of S1PR2 promotes inflammatory skin disease, it also increases permeability to pathogens and promotes infections.